Effective Health Care

Effectiveness of Treatments for Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD)

Results of Topic Selection Process & Next Steps

The nominator, the American College of Obstetrics and Gynecology (ACOG), is interested in using a new systematic review to examine the effectiveness and comparativeness effectiveness of treatments for PMS and PMDD to inform a practice guideline. The nominator states that an AHRQ product would provide the necessary information for clinicians to make appropriate treatment decisions for women with PMS or PMDD. Due to limited program resources, the program will not develop a review at this time. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Effectiveness of Treatments for Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD)

Topic #: 0649

Nomination Date: 06/23/2015

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Summary of Key Findings:

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: An evidence review on treatments for PMS and PMDD would not be duplicative.
    - The search for existing evidence retrieved fifteen systematic reviews since 2005. Four of these are Cochrane reviews. However, there is not a single comprehensive systematic review that examines all treatment options for PMS or PMDD.
- Impact: The nomination has high impact potential due to the lack of current, consistent, and comprehensive guidance on the benefits and harms of treatments for PMS and PMDD.
- Feasibility: A new evidence review on treatment options for PMS and PMDD is feasible at this time.
    - The search of PubMed retrieved 32 published studies and 20 listed studies on ClinicalTrials.gov on PMS and/or PMDD. The majority of the studies examine non-pharmacologic treatments for PMS, in particular, herbal and

dietary supplements. Few studies examine treatment options that are specifically targeted to the PMDD population.

- Value: The potential for value is high, given that ACOG will use a new AHRQ evidence review to inform a clinical practice guideline.

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Introduction

Premenstrual syndrome (PMS) is a collection of physical and psychological symptoms that start about 7 to 10 days before a woman gets her monthly period (menstruation). Many women experience breast tenderness and abdominal pain. Other symptoms can include headaches, back pain and joint or muscle aches, water retention (bloating), sleeping problems, digestive problems, changes in mood, decreased concentration, and anxiety.[1]

Premenstrual dysphoric disorder (PMDD) is a severe and debilitating form of PMS. Five or more symptoms must be present to diagnose PMDD, including one of many mood-related symptoms, ranging from trouble concentrating to panic attacks. Like PMS, PMDD follows a predictable, cyclic pattern. Symptoms begin in the late luteal phase of the menstrual cycle (after ovulation), about 1 week before menstruation, and ends shortly after menstruation begins.[1]

Because the etiologies of PMS and PMDD are not clear, the goal of treatment is symptom relief. General treatment strategies address the proposed physiologic causes of symptoms, such as the ovulatory hormonal cyclicity of menstruation or the central nervous system neurotransmitters affecting mood (e.g., serotonin). Hormonal treatments, including combined oral contraceptive pills, GnRH analogues, progestogens, estradiol, have been used for PMS and PMDD since the 1980's. They work by inhibiting ovulation, but their use may be inconsistent with the patient's fertility goals. Current treatments for PMS and PMDD symptoms include:

- Diet modifications
- Nutritional supplements such as vitamin B6, calcium, and magnesium
- Exercise
- SSRIs for mood symptoms. Fluoxetine, sertraline, and paroxetine are FDA approved for the treatment of PMDD.
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Diuretics
- Hormonal contraceptives
- Cognitive behavioral therapy (CBT)

In some cases, bilateral salpingo-oophorectomy (removal of the fallopian tube and ovary), with hysterectomy has been shown to decrease severe premenstrual symptoms when other treatments have failed. Bilateral salpingo-oophorectomy is not commonly considered as a treatment option for PMS or PMDD in clinical practice.[2]

There is uncertainty regarding the effectiveness and safety of treatment options for PMS and PMDD.

Topic nomination #0649 was received on June 23, 2015. It was nominated by the American College of Obstetrics and Gynecology. The questions for this nomination are:

Key Question 1. What is the effectiveness, including harms, of the following treatments compared with no treatment or other treatments for symptoms of PMS?

a. Non-pharmacologic
    i. Aerobic exercise
    ii. Dietary changes
    iii. Complementary and alternative therapies (e.g., nutritional supplements, herbal remedies, and acupuncture)
b. Pharmacologic
    i. Selective serotonin reuptake inhibitors (SSRIs)
    ii. Oral contraceptives
    iii. Gonadotropin-releasing hormone agonists
    iv. Other pharmacologic treatments

c. Behavioral
    i. Cognitive–behavioral therapy
d. Surgical
    i. Bilateral salpingo-oophorectomy

To define the inclusion criteria for the key questions, we specify the population, interventions, " comparators, and outcomes (PICOs) of interest. See Table 1. "

Table 1. Key Questions and PICOs "

Key Questions	1. What is the effectiveness, including harms, of the following treatments compared with no treatment or other treatments for symptoms of PMS? a. Non-pharmacologic i. Aerobic exercise ii. Dietary changes iii. Complementary and alternative therapies (e.g., nutritional supplements, herbal remedies, and acupuncture) b. Pharmacologic i. Selective serotonin reuptake inhibitors (SSRIs) ii. Oral contraceptives iii. Gonadotropin-releasing hormone agonists iv. Other pharmacologic treatments c. Behavioral i. Cognitive–behavioral therapy d. Surgical i. Bilateral salpingo-oophorectomy	2. What is the effectiveness, including harms, of the treatments outlined in the first question compared with no treatment or other treatments for symptoms of PMDD?
Population	Women of reproductive age diagnosed with premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD)	Women of reproductive age diagnosed with premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD)
Interventions	Non-pharmacologic (aerobic exercise, dietary supplementation, complementary and alternative therapies); pharmacologic (SSRIs, oral contraceptives, gonadotropin-releasing hormone agonists, other); surgical (bilateral salpingo-oophorectomy)	Non-pharmacologic (aerobic exercise, dietary supplementation, complementary and alternative therapies; pharmacologic (SSRIs, oral contraceptives, gonadotropin-releasing hormone agonists, other); surgical (bilateral salpingo-oophorectomy)
Comparators	Combination of treatments, placebo, no treatment	Combination of treatments, placebo, no treatment
Outcomes	Improvement of PMS or PMDD symptoms, improved quality of life, adverse effects	Improvement of PMS or PMDD symptoms, improved quality of life, adverse effects

Abbreviations: PMDD= Premenstrual Dysphoric Disorder; PMS=Premenstrual Syndrome; SSRI=Selective-Serotonin Reuptake Inhibitor

Methods

To assess topic nomination 0649, Effectiveness of Treatments for Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD), for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. " Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. " Establish the overall *importance* of a potential topic as representing a health or " healthcare issue in the United States.
3. " Determine the *desirability of new evidence review* by examining whether a new " systematic review or other AHRQ product would be duplicative. "
4. " Assess the *potential impact* a new systematic review or other AHRQ product.
5. " Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. " Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Table 2 includes the citations for the reviews that were determined to address the key questions.

Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether a new review could influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.). See Appendix A.

Feasibility of New Evidence Review

We conducted a literature search in PubMed from June 2005 to June 2015. We reviewed all identified titles and abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review. See *Table 2, Feasibility Column, Size/Scope of Review* section for the citations of included studies.

We also searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Appendix B for the PubMed search strategy and links to the ClinicalTrials.gov search.

Value

We assessed the nomination for value (see Appendix A). We considered whether a partner organization could use the information from the proposed evidence review to facilitate evidence-based change; or the presence of clinical, consumer, or policymaking context that is amenable to evidence-based change.

Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

Results

Appropriateness and Importance

This is an appropriate and important topic. This topic is of high public interest since approximately 20–30% of women report recurrent premenstrual symptoms in line with a diagnosis of mild to moderate PMS that can affect daily functioning.[3] Additionally, as many as 8% of women may experience PMDD symptoms, a more severe and potentially debilitating form of PMS.[4]

Desirability of New Review/Duplication

A new evidence review examining treatments for PMS and PMDD would not be duplicative of an existing product. The search for existing evidence retrieved fifteen systematic reviews since 2005.[5-19] Four of these are Cochrane reviews.[11,14-16] However, there is not a single comprehensive systematic review that examines all treatment options for PMS or PMDD. We did not identify systematic reviews related to exercise and dietary interventions (KQ 1ai, 1aii); and bilateral salpingo-oophrectomy (KQ1d). See Table 2, Duplication column for the systematic review citations that were determined to address the key questions.

Impact of a New Evidence Review

The nomination has high impact potential due to uncertainty in the standard of care across the available treatment options, and knowledge gaps identified in existing systematic reviews.

Feasibility of a New Evidence Review

A new evidence review examining treatments for PMS and PMDD is feasible. Although much of the new evidence retrieved by the feasibility scan is comprised of unique interventions and comparators, the development of an EHC product is feasible. The search of PubMed retrieved 32 published studies and 20 listed studies on ClinicalTrials.gov on PMS and/or PMDD. The majority of the studies (14) examine non-pharmacologic treatments for PMS, [20-33] in particular, herbal and dietary supplements. Few studies examine treatment options that are specifically targeted to the PMDD population. Five examine pharmacologic options for treating PMS/PMDD,[33-37] two look at cognitive behavioral therapy,[38,39] and no studies were identified for bilateral salpingo-oophorectomy as a treatment option for PMS/PMDD. See Table 2, Feasibility column for the citations that were determined to address the key questions.

Table 2. Key questions with the identified corresponding evidence reviews and original research

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing)
KQ 1a.i: Nonpharmacological—aerobic exercise	Total number of completed or in-progress evidence reviews – None identified.	Published Relevant Studies Identified: 1 • RCT – 1[20] Ongoing Relevant Trials: None
KQ 1a.ii: Nonpharmacological—dietary changes	Total number of completed or in-progress evidence reviews – None identified.	Published Relevant Studies Identified: 0 Ongoing Relevant Trials: None
KQ 1a.iii: Nonpharmacological—complementary and alternative therapies	Total number of completed or in-progress evidence reviews – 6[5-10] • Other – 6[5-10]	Published Relevant Studies Identified: 13 • RCT – 12[21-32] • Retrospective Cohort – 1[33] Ongoing Relevant Trials: 2 • Complete – 2[40,41]
KQ 1b.i:	Total number of completed or in-	Published

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing)
Pharmacologic—selective serotonin reuptake inhibitors (SSRIs)	progress evidence reviews – 4[6,11-13] • Cochrane – 1[11] • Other – 3[6,12,13]	Relevant Studies Identified: 5 • RCT – 4[34-37] • Retrospective Cohort – 1[33] Ongoing Relevant Trials: 5 • Recruiting – 2[42,43] • Complete – 3[44-46]
KQ 1b.ii: Pharmacologic— oral contraceptives	Total number of completed or in-progress evidence reviews – 2[12,14] • Cochrane – 1[14] • Other – 1[12]	Published Relevant Studies Identified: 1 • Retrospective Cohort – 1[33] Ongoing Relevant Trials: 10 • Complete – 10[42,43,47-54]
KQ 1b.iii: Pharmacologic—gonadotropin-releasing hormone agonists	Total number of completed or in-progress evidence reviews – 1[15] • Cochrane – 1[15]	Published Relevant Studies Identified: 1 • Retrospective Cohort – 1[33] Ongoing Relevant Trials: None
KQ 1b.iv: Pharmacologic— other pharmacologic treatments	Total number of completed or in-progress evidence reviews – 1[16] • Cochrane – 1[16]	Published Relevant Studies Identified: 5 • RCT – 4[35,36,55,56] • Retrospective Cohort – 1[33] Ongoing Relevant Trials: 4 • Recruiting – 1[57] • Complete – 3[58-60]
KQ 1c: Behavioral—cognitive behavioral therapy (CBT)	Total number of completed or in-progress evidence reviews – 3[17-19] • Other – 3[17-19]	Published Relevant Studies Identified: 2 • RCT – 2[38,39] Ongoing Relevant Trials: 1 • Recruiting – 1[61]
KQ 1d: Surgical—bilateral salpingo-oophorectomy	Total number of completed or in-progress evidence reviews – None identified.	Published Relevant Studies Identified: 0 Ongoing Relevant Trials: None
KQ 2: Effectiveness and harms of above treatments	Total number of completed or in-progress evidence reviews – 5[5,6,13,17,18] • Other – 5[5,6,13,17,18]	Published Relevant Studies Identified: 11 • RCT – 11[56,62-71] Ongoing Relevant Trials: None

Abbreviations: KQ=Key Question; RCT=Randomized Controlled Trial

Value

The potential for value is high, given that ACOG will use a new AHRQ evidence review to inform a clinical practice guideline.

Summary of Findings

- Appropriateness and importance: The nomination is both appropriate and important.
- Duplication: An evidence review on treatments for PMS and PMDD would not be duplicative.
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- Impact: The nomination has high impact potential due to the lack of current, consistent, and comprehensive guidance on the benefits and harms of treatments for PMS and PMDD.
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    - The search of PubMed retrieved 32 published studies and 20 listed studies on ClinicalTrials.gov on PMS and/or PMDD. The majority of the studies examine non-pharmacologic treatments for PMS, in particular, herbal and dietary supplements. Few studies examine treatment options that are specifically targeted to the PMDD population.
- Value: The potential for value is high, given that ACOG will use a new AHRQ evidence review to inform a clinical practice guideline.

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69. " Wu KY, Liu CY, Hsiao MC. Six-month paroxetine treatment of premenstrual dysphoric disorder: continuous versus intermittent treatment protocols. *Psychiatry Clin Neurosci.* Feb 2008;62(1):109-114.
70. " Yonkers KA, Brown C, Pearlstein TB, Foegh M, Sampson-Landers C, Rapkin A. Efficacy of a new low-dose oral contraceptive with drospirenone in premenstrual dysphoric disorder. *Obstetrics and gynecology.* Sep 2005;106(3):492-501.
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Appendices

Appendix A: Selection Criteria Summary !

Appendix B: Search Strategy & Results (Feasibility)

Appendix A. Selection Criteria Summary (

Selection Criteria	Supporting Data
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents a health care drug and intervention available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. ACOG states that approximately 20–30% of women report recurrent premenstrual symptoms in line with a diagnosis of mild to moderate PMS that can affect daily functioning.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, this topic affects heath care decisions for a large, vulnerable population and there is not a clearly established indication for treatment.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both the benefits and harms of various treatments for PMS and PMDD.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, this topic represents a common affliction, and the increasing medical care costs of its treatments.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	The search for existing evidence retrieved fifteen systematic reviews since 2005. Four of these are Cochrane reviews. However, there is not a single comprehensive systematic review that examines all treatment options for PMS or PMDD. There is also a lack of evidence-based guidelines that specifically point to treatment options for PMS or PMDD. There were no federal products that specifically examine treatment options for PMS or PMDD.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, the standard of care is unclear, and knowledge gaps may be addressed by a new evidence review.

4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, there is practice variation, and a new guideline will be aimed at gynecologists.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	Although much of the new evidence retrieved by the feasibility scan is comprised of unique interventions and comparators, the development of an EHC product is feasible. The search of PubMed retrieved 32 published studies and 20 listed studies on ClinicalTrials.gov on PMS and/or PMDD. The majority of the studies examine non-pharmacologic treatments for PMS, in particular, herbal and dietary supplements. Few studies examine treatment options that are specifically targeted to the PMDD population.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, this topic exists within a clinical and policy-making context that is amendable to evidence-based change.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes ACOG will disseminate the evidence-based treatments as a clinical recommendation.

Abbreviations: ACOG= American College of Obstetricians and Gynecologists; AHRQ=Agency for Healthcare Research and Quality; EHC=Effective Healthcare; PMDD= Premenstrual Dysphoric Disorder; PMS=Premenstrual Syndrome

Appendix B. Search Strategy & Results (Feasibility)

Source	Evidence
Published primary research studies PubMed/MEDLINE Other applicable databases (e.g., CINAHL, PsycINFO)	**Non-pharmacological** • Khayat S, Fanaei H, Kheirkhah M, et al. Curcumin attenuates severity of premenstrual syndrome symptoms: A randomized, double-blind, placebo-controlled trial. Complement Ther Med. 2015 Jun;23(3):318-24. doi: 10.1016/j.ctim.2015.04.001. Epub 2015 Apr 9. PMID: 26051565 • Abdollahifard S, Rahmanian Koshkaki A, Moazamiyanfar R. The effects of vitamin B1 on ameliorating the premenstrual syndrome symptoms. Glob J Health Sci. 2014 Jul 29;6(6):144-53. doi: 10.5539/gjhs.v6n6p144. PMID: 25363099 • Taavoni S, Barkhordari F, Goushegir A, et al. Effect of Royal Jelly on premenstrual syndrome among Iranian medical sciences students: a randomized, triple-blind, placebo-controlled study. Complement Ther Med. 2014 Aug;22(4):601-6. doi: 10.1016/j.ctim.2014.05.004. Epub 2014 May 13. PMID: 25146061 • Sharma B, Misra R, Singh K, et al. Comparative study of effect of anuloma-viloma (pranayam) and yogic asanas in premenstrual syndrome. Indian J Physiol Pharmacol. 2013 Oct-Dec;57(4):384-9. PMID: 24968577 • Sharifi F, Simbar M, Mojab F,et al. Comparison of the effects of Matricaria chamomila (Chamomile) extract and mefenamic acid on the intensity of premenstrual syndrome. Complement Ther Clin Pract. 2014 Feb;20(1):81-8. doi: 10.1016/j.ctcp.2013.09.002.Epub 2013 Oct 9. PMID: 24439651 • Brownley KA, Girdler SS, Stout AL, et al. Chromium supplementation for menstrual cycle-related mood symptoms. J Diet Suppl. 2013 Dec;10(4):345-56. doi: 10.3109/19390211.2013.830678. PMID: 24237190 • Carvalho F, Weires K, Ebling M, et al. Effects of acupuncture on the symptoms of anxiety and depression caused by premenstrual dysphoric disorder. Acupunct Med. 2013 Dec;31(4):358-63. doi: 10.1136/acupmed-2013-010394. Epub 2013 Sep 12. PMID: 24029029 • Sohrabi N, Kashanian M, Ghafoori SS, et al. Evaluation of the effect of omega-3 fatty acids in the treatment of premenstrual syndrome: "a pilot trial". Complement Ther Med. 2013 Jun;21(3):141-6. doi: 10.1016/j.ctim.2012.12.008. Epub 2013 Jan 16. PMID: 23642943 • Zamani M, Neghab N, Torabian S. Therapeutic effect of Vitex agnus castus in patients with premenstrual syndrome. Acta Med Iran. 2012;50(2):101-6. PMID: 22359078 • Canning S, Waterman M, Orsi N, et al. The efficacy of Hypericum perforatum (St John's wort) for the treatment of premenstrual syndrome: a randomized, double-blind, placebo-controlled trial. CNS Drugs. 2010 Mar;24(3):207-25. doi: 10.2165/11530120-000000000-00000. PMID: 20155996 • Ozgoli G, Selselei EA, Mojab F, et al. A randomized, placebo-controlled trial of Ginkgo biloba L. in treatment of premenstrual syndrome. J Altern Complement Med. 2009 Aug;15(8):845-51. doi: 10.1089/acm.2008.0493. PMID: 19678774 • Ghanbari Z, Haghollahi F, Shariat M,et al. Effects of calcium supplement therapy in women with premenstrual syndrome. Taiwan J Obstet Gynecol. 2009 Jun;48(2):124-9. doi: 10.1016/S1028-4559(09)60271-0. PMID: 19574172 • He Z, Chen R, Zhou Y, Geng L, et al. Treatment for premenstrual syndrome with Vitex agnus castus: A prospective, randomized, multi-center placebo controlled study in China. Maturitas. 2009 May 20;63(1):99-103. doi: 10.1016/j.maturitas.2009.01.006. Epub 2009 Mar 9. PMID: 19269753 • Gerhardsen G, Hansen AV, Killi M, et al. The efficacy of Femal in women with premenstrual syndrome: a randomised, double-blind, parallel-group, placebo-controlled, multicentre study. Adv Ther. 2008 Jun;25(6):595-607. doi: 10.1007/s12325-008-

Source	Evidence
	0072-4. PMID: 18568441 • Agha-Hosseini M, Kashani L, Aleyaseen A, et al. Crocus sativus L. (saffron) in the treatment of premenstrual syndrome: a double-blind, randomised and placebo-controlled trial. BJOG. 2008 Mar;115(4):515-9. doi: 10.1111/j.1471-0528.2007.01652.x. PMID: 18271889 **Pharmacologic** • Yonkers KA, Pearlstein TB, Gotman N. A pilot study to compare fluoxetine, calcium, and placebo in the treatment of premenstrual syndrome. J Clin Psychopharmacol. 2013 Oct;33(5):614-20. doi: 10.1097/JCP.0b013e31829c7697. PMID: 23963058 • Nazari H, Yari F, Jariani M,et al. Premenstrual syndrome: a single-blind study of treatment with buspirone versus fluoxetine. Arch Gynecol Obstet. 2013 Mar;287(3):469-72. doi: 10.1007/s00404-012-2594-x. Epub 2012 Oct 17. PMID: 23073723 • Freeman EW, Rickels K, Sammel MD, et al. Time to relapse after short- or long-term treatment of severe premenstrual syndrome with sertraline. Arch Gen Psychiatry. 2009 May;66(5):537-44. doi:10.1001/archgenpsychiatry.2008.547. PMID: 19414713 • Khajehei M, Abdali K, Parsanezhad ME, et al. Effect of treatment with dydrogesterone or calcium plus vitamin D on the severity of premenstrual syndrome. Int J Gynaecol Obstet. 2009 May;105(2):158-61. doi: 10.1016/j.ijgo.2009.01.016.Epub 2009 Feb 20. PMID: 19232611 • Steiner M, Ravindran AV, LeMelledo JM, et al. Luteal phase administration of paroxetine for the treatment of premenstrual dysphoric disorder: a randomized, double-blind, placebo-controlled trial in Canadian women. J Clin Psychiatry. 2008 Jun;69(6):991-8. PMID: 18517289 • Sharma P, Kulshreshtha S, Singh GM, et al. Role of bromocriptine and pyridoxine in premenstrual tension syndrome. Indian J Physiol Pharmacol. 2007 Oct-Dec;51(4):368-74. PMID: 18476391 • Wu KY, Liu CY, Hsiao MC. Six-month paroxetine treatment of premenstrual dysphoric disorder: continuous versus intermittent treatment protocols. Psychiatry Clin Neurosci. 2008 Feb;62(1):109-14. doi:10.1111/j.1440-1819.2007.01785.x. PMID: 18289149 • Landén M, Nissbrandt H, Allgulander C, et al. Placebo-controlled trial comparing intermittent and continuous paroxetine in premenstrual dysphoric disorder. Neuropsychopharmacology. 2007 Jan;32(1):153-61. Epub 2006 Oct 11. PMID: 17035933 • Contreras CM, Azamar-Arizmendi G, Saavedra M, et al. A five-day gradual reduction regimen of chlormadinone reduces premenstrual anxiety and depression: a pilot study. Arch Med Res. 2006 Oct;37(7):907-13. PMID: 16971235 • Pearlstein TB, Bachmann GA, Zacur HA, et al. Treatment of premenstrual dysphoric disorder with a new drospirenone-containing oral contraceptive formulation. Contraception. 2005 Dec;72(6):414-21. Epub 2005 Nov 2. PMID: 16307962 • Yonkers KA, Brown C, Pearlstein TB, et al. Efficacy of a new low-dose oral contraceptive with drospirenone in premenstrual dysphoric disorder. Obstet Gynecol. 2005 Sep;106(3):492-501. PMID: 16135578 **Behavioral** • Taghizadeh Z, Shirmohammadi M, Feizi A, et al.The effect of cognitive behavioural psycho-education on premenstrual syndrome and related symptoms. J Psychiatr Ment Health Nurs. 2013 Oct;20(8):705-13. doi:10.1111/j.1365-2850.2012.01965.x. Epub 2012 Sep 10. PMID: 22957993

Source	Evidence
Clinical trials ClinicalTrials.gov http://clinicaltrials.gov/ct2/search	**Completed** • NCT ID: NCT01782040 Title: Auriculotherapy in the Cares to the Premenstrual Syndrome Status: Completed (2013) o Condition: Premenstrual Syndrome o Intervention: Auriculotherapy group (non-pharmacological) • NCT ID: NCT02089620 Title: Comparison Between Oral Contraceptive Pills and Calcium Supplements in Treatment of Premenstrual Syndrome (PMS) Status: Completed (August, 2015) o Condition: Premenstrual Syndrome o Intervention: Yasmin; calver (pharmacological) • NCT ID: NCT02002182 Title: Comparison of Fluoxetine, Calcium and Placebo for the Treatment of Moderate to Severe Premenstrual Syndrome (PMS) Status: Completed (February 2015) o Condition: Premenstrual Syndrome o Intervention: Fluoxetine; calcium (pharmacological) • NCT ID: NCT00048854 Title: Antidepressant Treatment for Premenstrual Syndrome and Premenstrual Dysphoric Disorder Status: Completed (August, 2012) o Condition: Premenstrual Syndrome o Intervention: Sertraline • NCT ID: NCT00672607 Title: a Clinical Trial to Evaluate the Efficacy and Safety of Agnucaston Tablets in the Treatment of Premenstrual Syndrome (PMS) (ACT-RCT-C 01) Status: Completed (September, 2009) o Condition: Premenstrual Syndrome o Intervention: Extracts of Vitex agnus castus tablets • NCT ID: NCT00318773 Title: Short-Term Versus Long-Term Treatment for Severe Premenstrual Syndrome (PMS) Status: Completed (April, 2009) o Condition: Premenstrual Syndrome o Intervention: sertraline • NCT ID: NCT00128934 Title: Study Evaluating Combination of Levonorgestrel (LNG) and Ethinyl Estradiol (EE) in Premenstrual Dysphoric Disorder Status: Completed (April, 2007) o Condition: Premenstrual Syndrome o Intervention: levonorgestrel/ethinyl estradiol • NCT ID: NCT00195559 Title: Study Evaluating Combination of Levonorgestrel and Ethinyl Estradiol in Pre-Menstrual Dysphoric Disorder Status: Completed (December, 2007) o Condition: Premenstrual Syndrome o Intervention: levonorgestrel/ethinyl estradiol • NCT ID: NCT00161681 Title: Study Evaluating Levonorgestrel/Ethinyl Estradiol (LNG/EE) in PMS

Source	Evidence
	Status: Completed (February, 2013) o Condition: Premenstrual Syndrome o Intervention: levonorgestrel/ethinyl estradiol • NCT ID: NCT00005011 Title: Combined Hormone Replacement in Menstrually-Related Mood Disorders Status: Completed (July, 2015) o Condition: Premenstrual Syndrome; o Intervention: Estrogen; progesterone • NCT ID: NCT00611923 Title: Effectiveness of Flutamide in Treating Women With Premenstrual Dysphoric Disorder Status: Completed (June, 2012) o Condition: Premenstrual Syndrome o Intervention: Flutamide • NCT ID: NCT01482338 Title: Premenstrual Symptoms Treatment Comparing Between Oral Contraceptives Containing Desogestrel and Drospirenone Status: Completed (March, 2012) o Condition: Premenstrual Syndrome o Intervention: desogestrel 150 mg; drospirenone 3 mg • NCT ID: NCT00633360 Title: The Oral Contraceptive Pill for Premenstrual Worsening of Depression Status: Completed (July, 2014) o Condition: Premenstrual Syndrome o Intervention: Drospirenone and ethinyl estradiol • NCT ID: NCT00082043 Title: Dutasteride to Treat Women With Menstrually Related Mood Disorders Status: Completed (May, 2015) o Condition: Premenstrual Syndrome o Intervention: Dutasteride • NCT ID: NCT00518570 Title: Levetiracetam in the Treatment of Patients With Premenstrual Dysphoric Disorder (PMDD) (pmdd) Status: Completed (August, 2007) o Condition: Premenstrual Dysphoric Disorder o Intervention: Levetiracetam • NCT ID: NCT00927095 Title Continuous Oral Contraceptive Treatment in Premenstrual Dysphoric Disorder (PMDD) Status: Completed (August, 2007) o Condition: Premenstrual Dysphoric Disorder o Intervention: 20 ug ethinyl estradiol + 3 mg drospirenone **Recruiting** • NCT ID: NCT01961479 Title: Treatment of Premenstrual Syndrome - Internet-based Self-help (praemensis) Status: Recruiting o Condition: Premenstrual Syndrome o Intervention: Internet-based CBT for patients with PMS

Source	Evidence
	• NCT ID: NCT02427334 Title: Dienogest Versus Luteal Phase Fluoxetine in the Management of Premenstrual Syndrome Status: Recruiting o Condition: Premenstrual Syndrome o Intervention: Dienogest; Fluoxetine • NCT ID: NCT02488538 Title: Combined Oral Contraceptives and Fluoxetine Versus Combined Oral Contraceptives in Severe Premenstrual Syndrome Status: Recruiting o Condition: Premenstrual Syndrome o Intervention: Combined oral contraceptives; fluoxetine • NCT ID: NCT01870687 Title: Efficacy and Safety of 20 mg (2 Tablets of 10mg)VAC BNO 1095 FCT on Cyclic Mastodynia and PMS Status: Recruiting o Condition: Premenstrual Syndrome o Intervention: 20mg VAC BNO 1095 FCT • NCT ID: NCT01302834 Title: Radiation Therapy With Cisplatin or Cetuximab in Treating Patients With Oropharyngeal Cancer Status: Recruiting o Condition: HPV Positive Oropharyngeal Squamous Cell Carcinoma o Intervention: Biological: cetuximab; Drug: cisplatin